

# Periprostetik Eklem Enfeksiyonu Tanısında C-Reaktif ve Procalcitonin Sensitivite ve Spesifiteleri

## C-Reactive Protein and Procalcitonin Sensitivity and Specificities in the Diagnosis of Periprosthetic Joint Infections

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### ÖZ

**GİRİŞ ve AMAÇ:** Periprostetik enfeksiyonların tanısında laboratuvar testlerinin değeri halen tartışmalıdır. Bu çalışmanın amacı enfekte total kalça ve diz artroplastisi hastalarında pozitif ve negatif mikrobiyolojik kültür sonuçları ile mukayeseli olarak CRP ve PCT değerlerinin tanı koymadaki duyarlılık ve özgüllüğünü değerlendirmektir.

**YÖNTEM ve GEREÇLER:** Bu çalışmada enfekte total kalça veya total diz artroplastisi tanısı ile tedavi edilmiş toplam 40 hastanın klinik verileri retrospektif olarak değerlendirildi. Serum CRP ve PCT değerleri ile birlikte cerrahi olarak elde edilmiş mikrobiyolojik kültür sonuçları kaydedildi. Kültür sonuçları da pozitif ve negatif olarak sınıflandı. Buna göre her iki gruptaki hastalarda CRP ve PCT nin sensitivite ve spesifitesi değerlendirildi.

**BULGULAR:** Çalışmada elde edilen verilere göre periprostetik enfeksiyon tanısında CRP'nin duyarlılığı %100 ve özgüllüğü %52.6; PCT'nin ise duyarlılığı %85.7 ve özgüllüğü %95.7 tespit edilmiştir.

**TARTIŞMA ve SONUÇ:** CRP periprostetik enfeksiyon tanısında yüksek duyarlılığa PCT ise yüksek spesifiteye sahip değerli serolojik belirteçlerdir. Ortopedik cerrahlar periprostetik eklem enfeksiyonlarının tanısında bu iki belirteci göz önünde bulundurmalı ve gerekirse bir arada kullanmalıdır.

**Anahtar Kelimeler:** c-reaktif protein, prokalsitonin, periprostetik eklem enfeksiyonu

### ABSTRACT

**INTRODUCTION:** The value of laboratory tests in the diagnosis of periprosthetic infections is still controversial. The aim of this study was to evaluate the sensitivity and specificity of CRP and PCT values in comparison with the positive and negative microbiological culture results in infected total hip and knee arthroplasty patients.

**METHODS:** In this study, clinical data of a total of 40 patients with infected total hip or total knee arthroplasty were evaluated retrospectively. Microbiological culture results that were obtained surgically together with serum CRP and PCT values were recorded. Culture results were also classified as positive and negative. Accordingly, sensitivity and specificity of CRP and PCT were evaluated in both groups.

**RESULTS:** According to the data obtained in the study, the sensitivity of CRP in the diagnosis of periprosthetic infection was 100% and the specificity was 52.6%; PCT sensitivity was 85.7% and specificity was 95.7%.

**DISCUSSION and CONCLUSION:** CRP with high sensitivity and PCT with high specificity, are valuable serological markers with in the diagnosis of periprosthetic infection. Orthopedic surgeons should consider these two markers in the diagnosis of periprosthetic joint infections and use them together if necessary.

**Keywords:** c-reactive protein, procalcitonin, periprosthetic joint infection

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## INTRODUCTION

Periprosthetic infection is the most feared complication after total hip and knee arthroplasty (1,2). The rate of infection was reported as 2-4% in prosthetic surgeries and it was shown to be the cause of revision cases at approximately %15 (3,4). It is important to determine the presence of infection in patients with complaints and to distinguish whether the existing complaints are arising from septic or aseptic causes. The definitive diagnosis of periprosthetic joint infection is made by isolating the microorganism from the tissue sample in the culture medium. However, an infective agent cannot be isolated in approximately one third of cases (5). Therefore, in the presence of a clinical suspicion of infection, the primary diagnostic tool to be consulted by the physician during the initial evaluation of the patient is laboratory tests. C-reactive protein (CRP) is the most commonly used acute phase reactant in the diagnosis of periprosthetic joint infection (6, 7). CRP shows elevation in rheumatoid and inflammatory pathologies in many infections without bacterial or viral differentiation. Procalcitonin (PCT) is a marker composed of 116 amino acids produced by thyroid parafollicular cells and polymorphonuclear cells, and is increasingly recognized as specific of bacterial infections (6). Different rates are reported for the sensitivity and specificity of these two markers (7-9). The aim of this study was to evaluate the sensitivity and specificity of CRP and PCT values in comparison with the positive and negative microbiological culture results in infected total hip and knee arthroplasty patients.

## METHODS

In this study, clinical data of a total of 40 patients with infected total hip or total knee arthroplasty were evaluated retrospectively. 29 patients (72.5%) with infected total knee prosthesis and 11 patients (27.5%) with infected total hip prosthesis were included in the study. The mean age of the patients was 65 (between 52-86) years. There were 12 male and 28 female patients in the study group. All cases were unilateral and there were no patients with bilateral total prosthesis. 7 out of 11 hips were on the right, 4 were on the left and 18 out of 29 knees were on the right, and 11

were on the left side. All patients had periprosthetic infections after primary total joint prosthesis. The inclusion criteria were determined according to the guidelines set out in the standardized diagnostic guide published by the American Academy of Orthopedic Surgeons (AAOS) (Table 1). Exclusion criteria were the presence of infection after revision surgery, presence of systemic inflammatory disease, presence of coronary heart disease, presence of cancer, presence of rheumatic disease, continuous use of steroid, presence of active systemic infection. Of the 40 patients whose clinical data were evaluated, all had primary surgery with primary coxarthrosis or primary gonarthrosis diagnoses.

**Table 1. Periprosthetic joint Infection criterias defined by American Association of Orthopedic Surgeons (AAOS)**

|   |
|---|
| 1. Sinus tract communicating with the prosthesis  |
| 2. Positive culture from at least 2 separate tissue or fluid samples  |
| 3. Existence of 4 of the following 6 criteria: <ul style="list-style-type: none"> <li>• Serum ESR↑ and serum CRP↑</li> <li>• Synovial leukocyte count↑ and synovial neutrophil percentage (PMN%)↑</li> <li>• Purulence in the affected joint</li> <li>• Positive culture of periprosthetic tissue or fluid</li> <li>• &gt; 5 neutrophils per high-power field in 5 high-power fields in histologic analysis of periprosthetic tissue at 9400 magnification</li> </ul> |

The CRP and PCT values of all patients which were studied on the antecubital venous blood taken at the same day before the surgery, and the CRP and PCT values which were studied during the postoperative period due to clinical suspicion of infection were recorded. In addition, intraoperative deep surgical culture results obtained during surgical debridement, implant removal and application of antibiotic cement were evaluated in all patients. CRP values above 0.5 mg/dl and PCT values above 0.012 mg/dl were defined as positive test and values below were determined as negative tests. The microbiological culture results were also classified as non-reproductive sterile (culture negative) and reproductive (culture positive). Patients with positive microbiological culture and positive serological test results were reported as true positive, patients with negative microbiological culture and positive serological test results were reported as false negative.

Similarly, patients with negative microbiological culture and negative serological test results were reported as true negative, positive microbiological culture and negative serological test results were reported as false negative. Sensitivity and specificity ratios for CRP and PCT were calculated according to these definitions.

## RESULTS

In 4 (36.6%) of total 11 infected total hip arthroplasty patients, no bacterium could be produced in the microbiological culture made from deep tissue specimen taken during surgical debridement and implant removal, and the culture remained sterile. Similarly, in 15 patients (51.7%) of the 29 patients with infected total knee arthroplasty, there was no growth in surgical culture. Methicillin-resistant *Staphylococcus epidermidis* (MRSE) was the most frequently isolated bacteria in both hip and knee cases in positive microbiological cultures. Other agents are given in Table 2, respectively.

| Culture result  | Number of patients |
|---|--------------------|
| Meticilline resistant staphylococcus epidermidis (MRSE) | 6                  |
| Meticilline sensitive staphylococcus aureus (MSSA)      | 5                  |
| Meticilline resistant staphylococcus aureus (MRSA)      | 3                  |
| Meticilline sensitive staphylococcus epidermidis (MSSE) | 1                  |
| Enterobacter  | 1                  |
| Acinetobacter   | 1                  |
| Pseudomonas aeruginosa                                  | 1                  |
| Serratia marcescens                                     | 1                  |
| MRSA + Enterobacter                                     | 1                  |
| MRSA + MRSE   | 1                  |
| <b>Total</b>  | <b>21</b>          |

CRP and PCT values were noted within the normal values in all patients prior to primary hip or knee arthroplasty. In the clinical evaluation performed with the diagnosis of periprosthetic infection, in 30 out of 40 patients CRP was positive and 21 of those patients had positive and 9 had negative cultures when the serological test results, which were recorded prior to surgical debridement and implant removal operation, were

evaluated. PCT was positive in 19 patients and 18 of them were culture positive and 1 of them was culture negative patient. The sensitivity of CRP was found as 100%, specificity was 52.6%, PCT sensitivity was 85.7% and specificity was 94.7. In addition, the positive predictive value of CRP was 70%. The positive predictive value of PCT was found to be 94.7% with a negative predictive value of 85.7%. (Table 3).

|                     | Culture Positive | Culture Negative | Total     |
|---------------------|------------------|------------------|-----------|
| <b>CRP positive</b> | 21               | 9                | 30        |
| <b>CRP negative</b> | 0                | 10               | 10        |
| <b>Total</b>        | <b>21</b>        | <b>19</b>        | <b>40</b> |
|                     | Culture Positive | Culture Negative | Total     |
| <b>PCT positive</b> | 18               | 1                | 19        |
| <b>PCT negative</b> | 3                | 18               | 21        |
| <b>Total</b>        | <b>21</b>        | <b>19</b>        | <b>40</b> |

## DISCUSSION

The diagnosis of infection, which is one of the major complications after total joint prosthesis surgery, is vital for mortality and morbidity. Diagnosis is made with the clinical examination and laboratory tests and evaluation of the culture results. Today, there is no gold standard diagnostic method for periprosthetic joint infections. Pathogen may not be isolated by tissue culture, even in some cases of clinically indisputable periprosthetic joint infection (5). CRP, an acute phase protein produced by Interleukin-6 stimulation from the liver, is the most frequently used biomarker in the diagnosis of infection. Apart from bacterial infections, it can rise in viral and fungal infections, inflammatory pathologies, vasculitis, after trauma and surgery. However, PCT is thought to be specific for bacterial infections (5,6). Patients with cancer and coronary heart disease were not included in this study since PCT was reported to be elevated in some cases such as coronary heart disease and cancer. In addition, it was reported to be superior in the diagnosis of infections in the early phase, first two weeks, since its half-life is much shorter than CRP (10). Procalcitonin is a marker used to evaluate the diagnosis and treatment of sepsis and

to determine the prognosis and is becoming popular in the diagnosis of infections in other areas. When we look at previous studies on this group of patients, Yuan suggested that PCT was not superior to CRP in diagnosis (7). Similarly, Drago put forward this idea in his study (11). On the other hand, Bottner et al. reported the sensitivity of PCT as 0.33, specificity as 0.98, Ettinger et al. reported sensitivity as 0.90, specificity as 0.27; Glehr et al. reported sensitivity as 0.47, specificity as 1; Randau et al. reported sensitivity as 0.125 specificity as 1; Saeed et al. reported sensitivity as 0.75, spesificity as 0.83; Yuan et al reported sensitivity as 0.8 and specificity as 0.95 (7,8, 12-15). These results indicate that PCT has a high specificity against the sensitivity of the test and shows that the low false positivity is valuable in the diagnosis of infection. The data we have obtained in our study supports this. In a study evaluating the levels of erythrocyte sedimentation rate (ESR) and CRP in 131 infected total hip prostheses, the authors reported the sensitivity level of CRP as 94% (16). In another study, infected total knee prostheses were examined and it was emphasized that although the sensitivity of CRP was high, its specificity was low (17). According to the data obtained in our study, CRP values had high sensitivity in the diagnosis of periprosthetic joint infection and PCT values were found to have high specificity. Again, in cases where the microbiological culture remains sterile, the specificity levels of CRP is insufficient when the false positivity rate of serological tests is considered. Therefore, the combination of CRP and PCT should be considered as a more suitable option for making a diagnosis.

The retrospective research method and the relatively limited number of cases are the main limitations of this study. Furthermore, the absence of polymerase chain reaction (PCR) or sonication methods for the isolation of pathogen microorganism may be considered as another limitation. On the other hand, the evaluation of sensitivity and specificity levels of serological tests, based on surgical tissue cultures, allowed a more reliable analysis than joint aspiration.

## CONCLUSIONS

In conclusion, the combination of PCT and CRP in the diagnosis of periprosthetic infection may be more accurate when considering the sensitivity and specificity values. In addition to the high sensitivity of CRP, the high specificity of PCT will increase the success in diagnosing. However, prospective studies with higher number of patients should be performed.

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